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TITLE: Electromagnetic-Optical Coherence Tomography Guidance of Transbronchial Solitary Pulmonary Nodule Biopsy

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14. ABSTRACT

We present a novel high-resolution multimodality imaging platform utilizing CT and electromagnetic (EM) navigation for spatial guidance to targeted lung nodules, and OCT for microscopic volumetric imaging. The OCT optic fiber probe and EM sensor were incorporated into a single flexible catheter. The catheter was designed to be compatible with a custom peripheral transbronchial aspiration needle to enable both imaging and specimen collection. The EM sensor guides the catheter and biopsy needle to the spatial location of the pulmonary nodules and OCT images are obtained to microscopically assess the tissue.

15. SUBJECT TERMS

Electromagnetic Optical Coherence Tomography, Biopsy Guidance, Lung Cancer, Optical Microscopy

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1. INTRODUCTION

Lung cancer is the leading cause of cancer related death accounting for more deaths than breast, prostate and colon combined. Early diagnosis is critical to patient survival, however the vast majority of lung malignancies are detected only once symptoms arise and the cancer has spread, at which time patients have little chance of cure. Macroscopic imaging modalities including CT and bronchoscopy have made significant strides in increasing early detection, however they do not have the required specificity to diagnose malignancy. Diagnosis must be made on the microscopic level, which at present can only be accomplished with excisional biopsy. Unfortunately, low-risk bronchoscopic techniques for retrieving biopsy samples are hampered by low diagnostic yields, and trans-thoracic and surgical approaches carry higher intrinsic risk of complications. Given the very high false positive rates of these macroscopic imaging platforms it is imperative that high-risk procedures are avoided and the diagnostic accuracy of lower-risk approaches are greatly improved. In this proposal we aim to dramatically increase the diagnostic yield of low-risk bronchial biopsy using a novel multimodality electromagnetic and optical coherence tomography (EM-OCT) biopsy guidance platform to provide not only macroscopic spatial guidance to the lesion (using CT and EM) but to additionally confirm the needle placement within the lesion on the microscopic scale (OCT) ensuring that the needle is positioned within the target lesion prior to biopsy acquisition. Specifically we will (Aim 1) develop and fabricate an EM-OCT catheter, rotary junction and system software to facilitate real-time 3D imaging of, and navigation to, SPN for transbronchial biopsy, and (Aim 2) conduct a preclinical study to demonstrate the feasibility of EM-OCT biopsy guidance of artificial SPN (aSPN) in living swine.

2. KEYWORDS

Electromagnetic Navigation, Biopsy Guidance, Optical Microscopy, Optical Coherence Tomography, Lung Cancer, Optical needle.

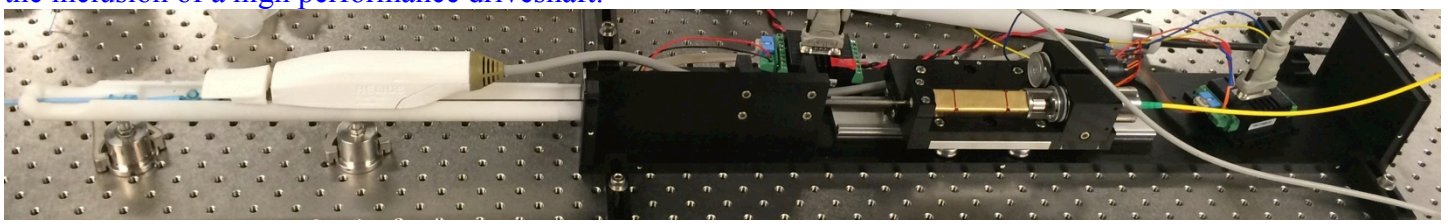
3. OVERALL PROJECT SUMMARY

***Aim 1:* Develop and fabricate an EM-OCT catheter, rotary junction, and system software to facilitate real-time 3D imaging of, and navigation to, peripheral pulmonary lesions for transbronchial biopsy.**

Task 1: Construct and electro-optical rotary junction

1a: Design and fabricate a high speed, high signal throughput optical rotary junction including electrical slip rings to convey the EM sensor information

We have fabricated the electo-optical rotary joint. During this process we ran into issues with non-uniform rotation and electrical noise, which were successfully overcome with repositioning of the DC motors, and the inclusion of a high performance driveshaft.



Picture of the electro-optical rotary junction with case removed.

1b: Design and fabricate the rapid-connect joint to attach the EM-OCT catheter to the electro-optical rotary junction.

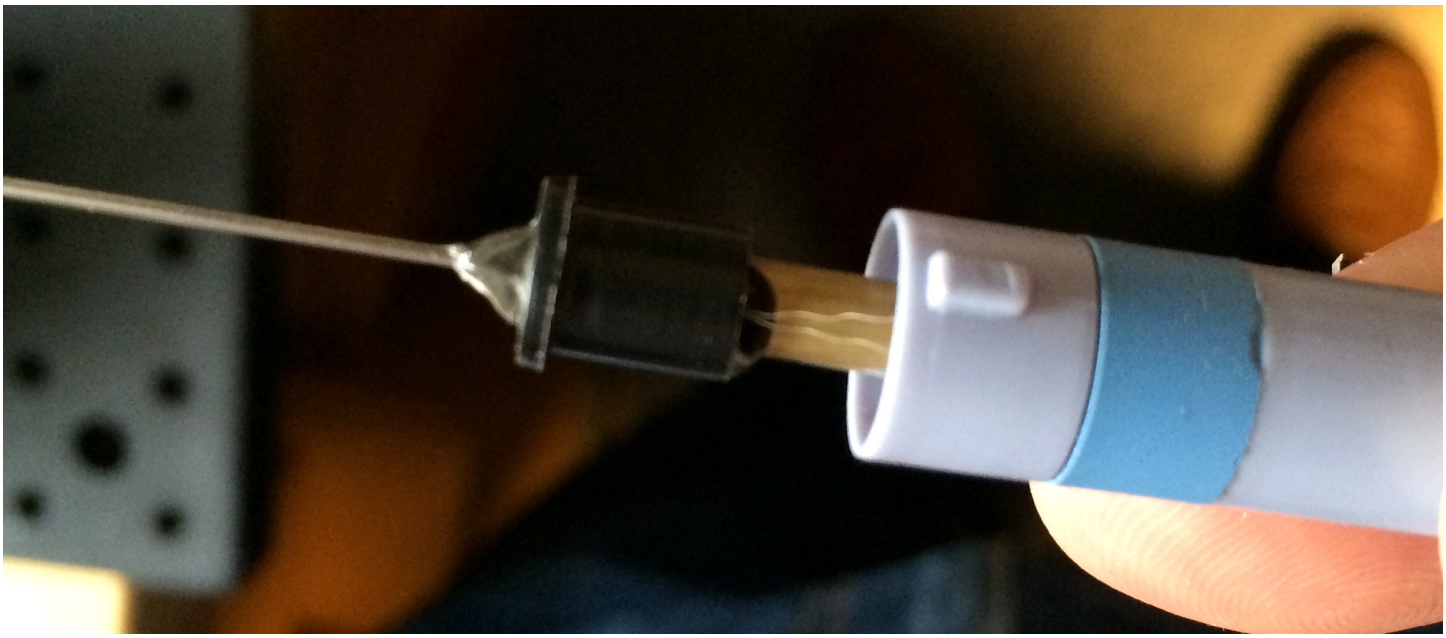
We have designed and fabricated the rapid-connect joint for the catheter. The elegant design eliminates the need for careful alignment by the physician/operator during the procedure as is currently necessary with our existing OCT imaging catheters.

This is an image of the rapid connect design highlighting the circumferential symmetry of the connector for ease of use.

Task 2: Design and construct EM-OCT catheters that are compatible with standard TBNA

2a: Fabricate a number of optical imaging cores based on our existing ball lens design

We have fabricated a total of 15 inner optical cores using a small monolithic ball lens design to achieve a focus of 25-30 microns at a focal length of 600 microns

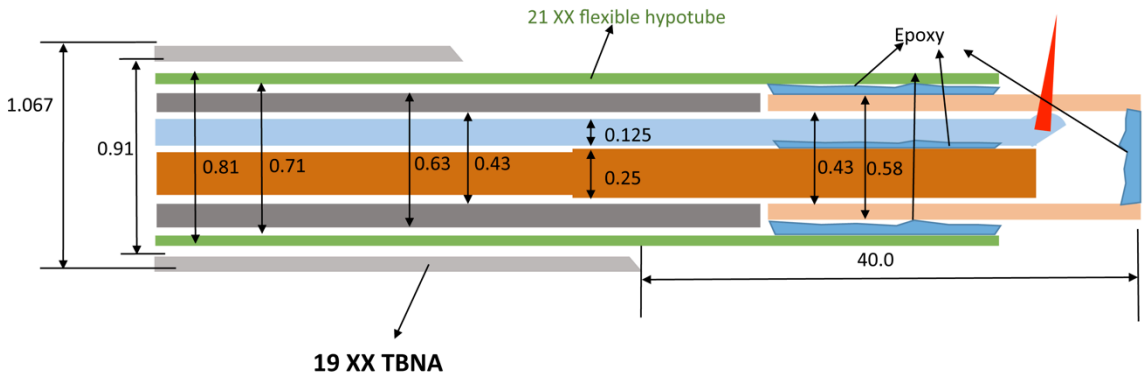


Above is a picture of the proximal end of the EM-OCT catheter showing both the optical imaging core and the two wires that lead to the EM sensor located at the distal end of the catheter.

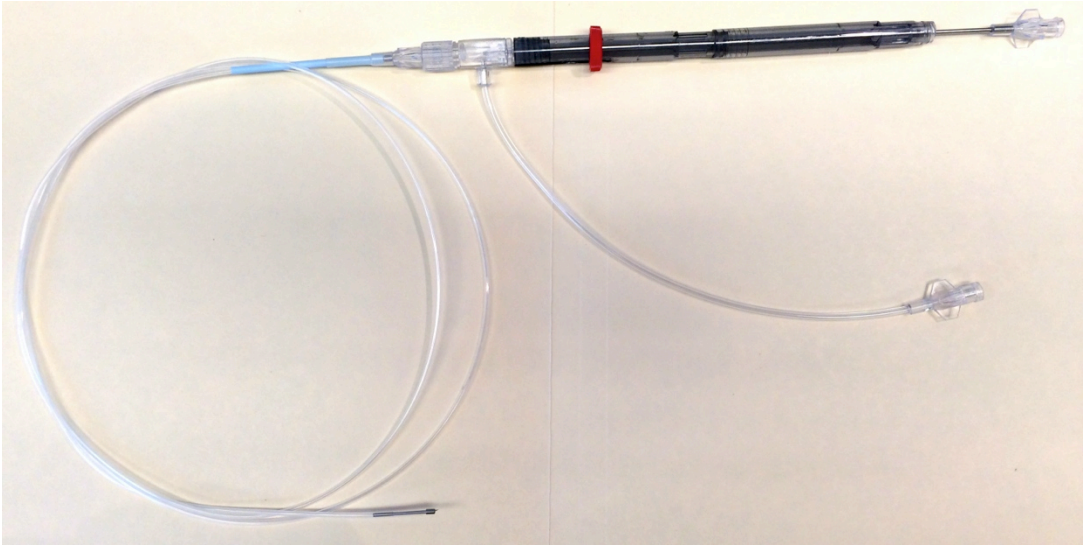
2b: Assemble the EM-OCT catheter ensuring accurate sensor positioning distal to the imaging optics

We have ordered and received all of the components for the EM-OCT catheters including the torque coils, EM sensors, and transbronchial needles. We have fabricated 2 prototype OCT needle catheters. We did overcome a number of challenges during this process.

- We modified the design of the inner OCT core to include a metallic coating with a distal transparent window for OCT imaging. The optics and sensor will rotate together independently of the protective sheath and the entire assembly will translate within the needle to facilitate spiral cross-sectional imaging of the nodules.



- TBNA needles with a stylet are no longer commercially available. We have developed custom TBNA needles to interface with our EM-OCT catheter for this study.



The above photograph is of our custom TBNA needle.

- One of the assembled catheters failed testing. We are currently in the process of testing the 2nd.

2c: Test the optical and electrical performance and calibrate the precise optical viewing angle and EM sensor position for each catheter.

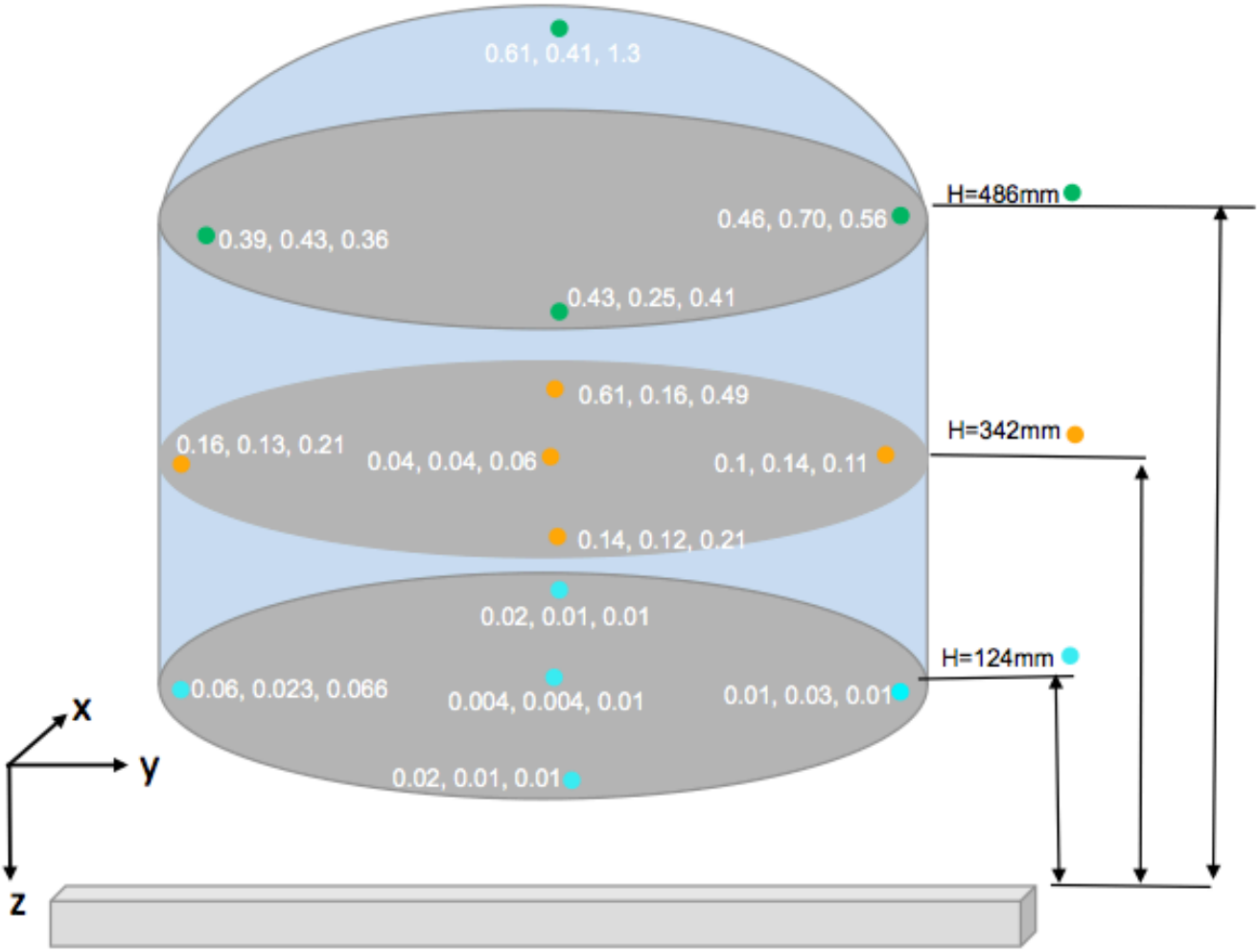
We have performed extensive testing of each of the sensors and the optical imaging cores seperately. Upon final assembly, each catheter will be again tested and carefully calibrated to accommodate minor offsets in OCT imaging window and sensor position.

Testing of the NDI Aurora tabletop system with a 5 degrees of fredom sensor (0.3mm x 13 mm), 40 Hz update rate:

Working volume: 420 mm x 600 mm x 480 mm

Orientation angle error: <0.1 degree

Spatial Error as shown below

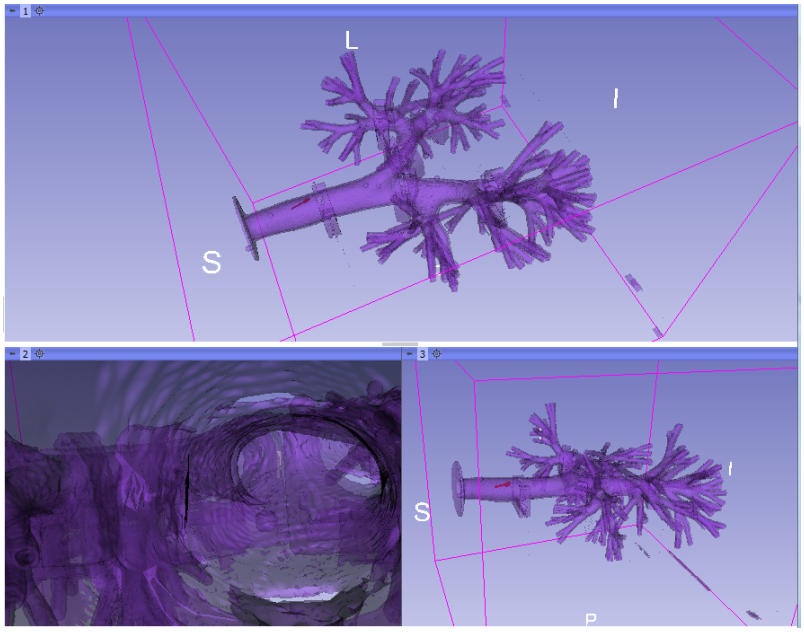


Task 3: Design and develop navigational software to provide real time tracking of the catheter position within the tracheobronchial tree

3a: Modify an existing OCT system to simultaneously record the catheter position data associated with each OCT image axial depth profile.

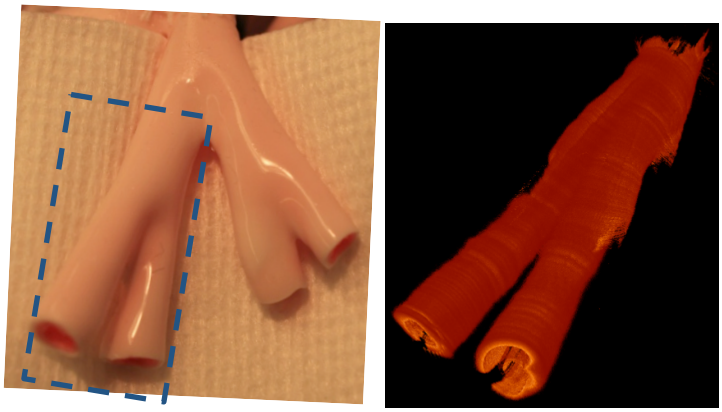
Rather than save the EM sensor data on the OCT system as originally designed, we synchronized two separate systems to ensure that we can maintain the necessary write speeds for both modalities. The OCT system sends a trigger to the Aurora Tracking system to commense saving and control of the EM-OCT catheter scanning. Software has been modified to display the position of the sensor within the tracheobronchial tree in real time (see below).

3b: Modify existing electromagnetic navigation software to track the catheter position within the tracheobronchial tree using in real time.



We have written software to track the sensor/catheter position within the 3D volume (rendered from CT) in real-time. Cursors show the position of the catheter.

3c: Develop software to construct multi-modality CT and OCT images of the airways using the registered datasets to provide a synergistic description of the lung and tumor environment and to precisely localize biopsy acquisition location.



We have successfully used the EM information to perform accurate 3D renderings of the OCT images (see images above). However, we have not yet constructed multi-modality images.

<u>Aim 2:</u> Conduct a preclinical study to demonstrate feasibility of EM-OCT biopsy guidance of artificial SPN (aSPN) in living swine (n=6).

<u>Task 4: Validation and refinement of catheter tracking within fixed lungs</u>

4a: Freshly excised lungs (n=2) will be obtained from swine and will be fixed using the modified Heitzman procedure to maintain radio-opacity on CT and OCT imaging.

We have harvested and fixed 1 set of lungs according to the protocol outlined in the original grant. We have additionally purchased an airway phantom for quick in-lab testing of the softeware platform.

4b: Artificial solitary pulmonary nodules (aSPN) consisting of agar, barium sulfate and microspheres will be injected transpleurally into random locations within the fixed lungs. The lung will be secured within a black box, CT imaging will be performed, and the airway tree and nodules locations will be mapped.

We have refined the procedure for generating the aSPN. We have successfully injected them into the fixed lung (4a) and have additionally acquired a CT scan of the lung verifying the visibility of the aSPN.

4c: Transbronchial needle biopsies of the artificial nodules will be acquired using the EM-OCT biopsy guidance platform and standard EBUS guided biopsy. Biopsy accuracy and displacement errors will be calculated and statistically compared.

We will be conducting the biopsy study in the coming months following the completion and testing of additional EM-OCT catheters. We have preliminarily conducted this step using one of our OCT needle catheters without EM guidance capabilities.

Task 5: Conduct swine studies to demonstrate the feasibility of EM-OCT transbronchial biopsy guidance and to determine the potential increase in the diagnostic yield over conventional biopsy approaches.

We have not yet commenced the in vivo swine study

4. KEY RESEARCH ACCOMPLISHMENTS

Nothing to report.

5. CONCLUSION

We have accomplished many of the milestones outlined above for this research proposal and do not expect any difficulties completing the tasks as outlined in the statement of work.

Our objective is to develop, test and validate an EM-OCT biopsy guidance platform that is compatible with standard bronchoscopy techniques and greatly increases the diagnostic yield of bronchial biopsy. This objective is in line with the following LCRP Area of Emphasis: ***"Identification or development of non-invasive or minimally invasive tools to improve detection of the initial stages of lung cancer."*** Increasing the diagnostic yield of transbronchial biopsy approaches may reduce the number of high-risk surgical diagnostic procedures performed, and when coupled with CT screening may increase the early detection of lung cancer.

Specifically we envision that following the identification and gross localization of a nodule by CT, a low-risk transbronchial biopsy will be acquired for diagnosis using EM-OCT guidance rather than a higher-risk transthoracic or surgical diagnostic procedure. The EM-OCT biopsy guidance platform will (1) provide spatial guidance to the lesion through real-time tracking the location of the biopsy needle within the lung using the previously reconstructed CT roadmap of the tracheobronchial tree, and (2) will provide microscopic OCT guidance to ensure that the needle is positioned within the lesion prior to biopsy acquisition.

6. PUBLICATIONS, ABSTRACTS AND PRESENTATIONS

Abstract/Oral Presentation:

1. Wang Y, Jagadeesan J, Adams DC, Miller AJ, Hariri LP, Vosburg K, Suter MJ. Electromagnetic optical coherence tomography for assessment of the pulmonary airways. SPIE Photonics West; 2014 February, San Francisco, CA USA: 8927-41.

7. INVENTIONS, PATENTS AND LICENSES

Nothing to report.

8. REPORTABLE OUTCOMES

Nothing to report.

9. OTHER ACHIEVEMENTS

Nothing to report.

10. REFERENCES

None

11. APPENDICES

None

SUPPORTING DATA

None